Claims

1. A substance capable to block or modify endogenous CD_{1d} function, obtainable by a process comprising the steps of :
   (a) exposing epithelial cells to a substance of interest,
   (b) subjecting the epithelial cells to a stress situation,
   (c) determining the effect of said stress to said epithelial cells by screening for one or more of the following assays,
      (i) epithelial hyperplasia (H&E),
      (ii) epithelial proliferation (BrUd, PCNA),
      (iii) epithelial apoptosis (TUNEL),
      (iv) p53 mutation accumulation,
      (v) quantitative and qualitative assessment of epithelial lipids,
      (vi) co-clustering patterns of apoptotic and non-apoptotic cell surface receptors,
      (vii) production of pro-inflammatory cytokines,
      (viii) production of immuno-modulatory cytokines,
      (ix) markers of inflammation,
      (x) anti-apoptotic transcription factors,
      (xi) markers of ageing,
   (d) comparing the results obtained with a control.

2. The substance according to claim 1, which is capable of preventing and/or treating detrimental effects of stress to epithelial cells.

3. The substance according to claim 1, which is capable of preventing or treating hair loss.

4. The substance according to any of the preceding claims, which is a compound reducing the transcription and/or translation of the CD_{1d} gene.

5. The substance according to claim 4, which is a polynucleotide antisense to a sequence comprised by the CD_{1d}-gene and/or the CD_{1d}-mRNA.

6. The substance according to any of the claims 1 to 4, which is a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosyl-ceramide synthase mRNA.

7. The substance according to any of the claims 1 to 4, which is a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA.

8. The substance according to any of the claims 1 to 4, which is a polypeptide or peptide, binding to CD_{1d} and essentially blocking or modifying CD_{1d} function.

9. The substance according to claim 8, wherein the polypeptide is an antibody or the variable part of an antibody.

10. The substance according to any of the claims 1 to 4, which is a lipid.

11. The substance according to claim 10, wherein the lipid is a sphingolipid, glycosphingolipid, phospholipid, ganglioside, sterol, fatty acid, glyceride or phosphatidylinositol phosphate.

12. The substance according to claim 10 and 11 which is derived from plants, microbes or animals, or a phytochemicals, especially a natural or synthetic polyphenols, or ingredients of green tee, and a ginkolide, vitamin, amino acid or carotenoid.

13. The substance according to claim 8, which is a ceramide or a ligand of a receptor belonging to the TNF-superfamily, in particular CD95/APO-1/Fas.

14. The substance according to any of the preceding claims for the preparation of a carrier for the prevention and/or treatment of the detrimental effects of stress to epithelial cells

and/or hair loss.

15. A composition, containing at least a substance according to any of the preceding claims.

16. A composition according to claim 15, which is a food composition, a cosmetic composition or a pharmaceutical composition.

17. The composition according to claim 16, which is milk, yogurt, curd, cheese, fermented milks, milk based fermented products, ice-creams, milk based powders, infant formulae, cereal products, fermented cereal based products, mineral water, chocolate or pet food, or lotions, shampoos, creams, sun-screens, after-sun creams, anti-ageing creams and/or ointments or tablets, liquid, dried oral supplement, wet oral supplement, dry tube-feeding or wet tube-feeding or an anti-cancer drug.

18. Use of a substance according to any of the claims 1 to 14 or a composition according to any of the claims 13 to 15 for the prevention and/or treatment of damages in epithelial tissues produced by a stress situation and/or for the prevention and/or treatment of hair loss.

19. The use according to claim 18, wherein the stress, situation is a chemical stress, a biological stress or a physical stress.

20. The use according to any of the claims 19, wherein the chemical stress is exerted by exposure to oxidants or carcinogens, or wherein the biological stress is exerted by exposure to bacteria, viruses, fungi, lipids derived from surrounding cells and/or microbes, or wherein the physical stress is exerted by exposure to UV-irradiation.

21. The use according to any of the claims 18 to 20, wherein the damage is skin burning and/or blistering, cataract formation, epidermal hyperplasia, cancer, inflammation, immune suppression, skin ageing.

22. The use according to any of the claims 18 to 21, wherein the epithelial cells are derived from the skin, gut, eye, lung, prostate, liver, breast, kidney and/or the uterus.

23. The use according to claim 21, wherein the cancer is breast cancer, colon cancer, prostate cancer, liver cancer, pancreatic cancer, kidney cancer, non-melanoma and melanoma skin cancers.

24. A method for identifying CD_{1d} blocking or modifying substances, which comprises the following steps:

(a) exposing epithelial cells to a substance of interest,

(b) subjecting the epithelial cells to a stress situation,

(c) determining the effect of said stress to said epithelial cells by screening for one or more of the following assays,

(i) epithelial hyperplasia (H&E),

(ii) epithelial proliferation (BrUd, PCNA),

(iii) epithelial apoptosis (TUNEL),

(iv) p53 mutation accumulation,

(v) quantitative and qualitative assessment of epithelial lipids,

(vi) co-clustering patterns of apoptotic and non-apoptotic cell surface receptors,

(vii) production of pro-inflammatory cytokines,

(viii) production of immuno-modulatory cytokines,

(ix) markers of inflammation,

(x) anti-apoptotic transcription factors,

(xi) markers of ageing,

(d) comparing the results obtained with a control.

25. The method according to claim 24, wherein the stress situation is a chemical stress, a biological stress or a physical stress.

26. The method according to claim 25, wherein the chemical stress is exerted by exposure to oxidants or carcinogens, or wherein the biological stress is exerted by exposure to bacteria, viruses, fungi, lipids derived from surrounding cells and/or microbes, or wherein the physical stress is exerted by exposure to UV-irradiation.

27. The method according to claim 24 to 26, wherein the pro-inflammatory cytokines are selected from the group consisting of IL-1, TNF-α, PGE-2, IL-6, IFN-γ or IL-8.

28. The method according to any of the claims 24 to 26, wherein the immuno-modulatory cytokines are selected from the group consisting of PAF, IL-10, IL-4 or TGF-ß.

29. The method according to any of the claims 24 to 26, wherein the lipids are selected from the group consisting of phospholipids, sphingolipids and glycosphingolipids.

30. The method according to any of the claims 24 to 26, wherein the markers of inflammation include COX-2 and iNos.

31. The method according to any of the claims 24 to 26, wherein the anti-apoptotic transcription factors include AP-1 and NFkappaB.

32. The method according to any of the claims 24 to 26, wherein the markers of aging include elastases, collagenases, metalloproteinases, gelatinases, stromelysins, telomerases.

33. Use of a substance according to any of the claims 1 to 14 or a composition according to any of the claims 15 to 17 for decreasing multi-drug resistance of cancers.

34. The use according to claim 33, wherein the cancer is skin, gut or breast cancer.

35. Use of cells expressing and/or over-expressing CD_{1d} in an assay for screening for substances modifying and/or blocking CD_{1d} function.

36. Use of $CD_{1d}^{-/-}$ animals as a test model for determining the activity of substances influencing damages in epithelial tissues produced by a stress situation and/or hair loss.

37. Use of a substance according to any of the claims 1 to 14 in gene therapy.